

AMENDMENT

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

In the Specification:

Please replace page 15, line 32, to page 16, line 4, of the application with the following rewritten paragraphs:

-- Figure 32 shows aligned amino acid sequences of DSL domains from various Drosophila and mammalian Notch ligands (SEQ ID NO:18-33);

Figure 33 shows amino acid sequences of human Delta-1, Delta-3 and Delta-4 (SEQ ID NO:34-36);

Figure 34 shows amino acid sequences of human Jagged-1 and Jagged-2 (SEQ ID NO:37-38);

Figure 35 shows the amino acid sequence of human Notch1 (SEQ ID NO:39);

Figure 36 shows the amino acid sequence of human Notch2 (SEQ ID NO:40); --

Please replace page 40, line 28, to page 41, line 23, of the application with the following rewritten paragraphs:

-- A typical DSL domain may include most or all of the following consensus amino acid sequence:

Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa **Cys** Xaa Xaa Xaa **Cys** Xaa Xaa
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa **Cys** Xaa Xaa Xaa Xaa Xaa Xaa
Xaa **Cys** Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa **Cys** (SEQ ID NO:1)

Preferably the DSL domain may include most or all of the following consensus amino acid sequence:

Cys Xaa Xaa Xaa ARO ARO Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys BAS NOP
BAS ACM ACM Xaa ARO NOP ARO Xaa Xaa Cys Xaa Xaa Xaa NOP Xaa Xaa
Xaa Cys Xaa Xaa NOP ARO Xaa NOP Xaa Xaa Cys (SEQ ID NO:2)

wherein:

ARO is an aromatic amino acid residue, such as tyrosine, phenylalanine, tryptophan or histidine;

NOP is a non-polar amino acid residue such as glycine, alanine, proline, leucine, isoleucine or valine;

BAS is a basic amino acid residue such as arginine or lysine; and

ACM is an acid or amide amino acid residue such as aspartic acid, glutamic acid, asparagine or glutamine.

Preferably the DSL domain may include most or all of the following consensus amino acid sequence:

Cys Xaa Xaa Xaa Tyr Tyr Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys Arg Pro
Arg Asx Asp Xaa Phe Gly His Xaa Xaa Cys Xaa Xaa Xaa Gly Xaa Xaa
Xaa Cys Xaa Xaa Gly Trp Xaa Gly Xaa Xaa Cys (SEQ ID NO:3) --

Please replace page 43, lines 6-21, with the following rewritten paragraphs:

-- As reported by PROSITE the EGF domain typically includes six cysteine residues which have been shown (in EGF) to be involved in disulfide bonds. The main structure is proposed, but not necessarily required, to be a two-stranded beta-sheet followed by a loop to a C-terminal short two-stranded sheet. Subdomains between the conserved cysteines strongly vary in length as shown in the following schematic representation of the EGF-like domain (SEQ ID NO:4):

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+-----+
|               |               |
x(4)-C-x(0,48)-C-x(3,12)-C-x(1,70)-C-x(1,6)-C-x(2)-G-a-x(0,21)-G-x(2)-C-x
|               |               *****
+-----+

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wherein: --

Please replace page 104, lines 17-21, with the following rewritten paragraphs:

-- *mouse 18s rRNA*: **Forward** GTAACCCGTTGAACCCCAT (SEQ ID NO:5)
Reverse CCATCCAATCGGTAGTAGCG (SEQ ID NO:6)

mouse Hes-1: **Forward** GGTGCTGATAACAGCGGAAT (SEQ ID NO:7)
Reverse ATTTTGGGAATCCTTCACGC (SEQ ID NO:8) --

Please replace page 107, lines 7-19, with the following rewritten paragraphs:

-- **BglII** **HindIII**
GATCTGGGGGGCTATAAAAGGGGGTA (SEQ ID NO:9)
ACCCCCGATATTTTCCCCCATTCGA (SEQ ID NO:10)

This was cloned into plasmid pGL3-Basic (Promega) between the BglII and HindIII sites to generate plasmid pGL3-AdTATA.

A TP1 promoter sequence (TP1; equivalent to 2 CBF1 repeats) with BamH1 and BglII cohesive ends was generated as follows:

BamH1 BglII
5' GATCCCGACTCGTGGGAAAATGGGCGGAAGGGCACCGTGGGAAAATAGTA 3' (SEQ ID NO:11)
3' GGCTGAGCACCTTTTACCCGCCTTCCCGTGGCACCTTTTATCATCTAG 5' (SEQ ID NO:12) --

Please replace page 122, lines 19-20, with the following rewritten paragraphs:

-- hN1F: CAC CCC ATG GCT ACC TGT CAG (SEQ ID NO:13)
hN1R: GGC TGC ACC TGC TGG GTC TGC (SEQ ID NO:14) --

Please replace page 123, lines 7-10, with the following rewritten paragraphs:

-- hN1-IC1759: AAA GGA TTC ACC **ATG** GCA CGC AAG CGC CGG CGC AGT CAT
(SEQ ID NO:15) (contains initiation methionine in **bold**)
hN1-IC 2556: GCG CTC GAG *TTA* CTT GAA CGC CTC CGG GAT GCG (SEQ ID NO:16)
(contains stop codon in *italics*) --

Please replace page 123, line 31, to page 124, line 14, with the following rewritten paragraph:

-- MARKRRRQHGQLWFPEGFKVSEASKKKRREPLGEDSVGLKPLKNASDGALMDDNQ
NEWGDEDLETKKFRFEFPVVLPLDLDQTDHRQWTQQHLDAADLRMSAMAPTPPQGEV
DADCMDVNVVRGPDGFTPLMIASCSGGLETGNSEEEEDAPAVISDFIYQGASLHNQTDR
TGETALHLAARYSRSDAAKRLLEASADANIQDNMGRTPLHAAVSADAQGVFQILIRNR
ATDL DARMHDGTTPLILAAARLAVEGMLEDLINSHADVNAVDDLKGSALHWAAAVNNV
DAAVVLLKNGANKDMQNNREETPLFLAAREGSYETAKVLLDHFANRDITDHMDRLPR
DIAQERMHHDIVRLLDEYNLVRSPQLHGAPLGGTPTLSPPLCSPNGYLGSLKPGVQGGK
VRKPSSKGLACGSKEAKDLKARRKKSQDGKGCLLDSSGMLSPVDSLESPhGYLSDVAS
PPLLSPFQQSPSVPLNHLPGMPDTHLGIGHLNVAAPEMAALGGGGRLAFETGPPRLSH
LPVASGTSTVLGSSSGGALNFTVGGSTSLNGQCEWLSRLQSGMVPNQYNPLRGSVAPGP
LSTQAPSLQHGMVGPLHSSLAASALSQMMSYQGLPSTRLATQPHLVQTQQVQPQNLQM
QQQNLQPANIQQQQSLQPPPPPPQPHLGVSSAASGHLGRSFLSGEPSQADVQPLGPSSLA
VHTILPQESPALPTSLPSSLVPPVTAAQFLTPPSQHSYSSPVDNTPSHQLQVPEHPFLTPSP
ESPDQWSSSSPHSNVSDWSEGVSSPPTSMQSQIARIEAFK (SEQ ID NO:17) --

Please add the enclosed papers entitled --Sequence Listing-- after page 136 of the specification and before the claims.